

CLAIMS

We claim:

1. An isolated antibody comprising an amino acid sequence which is at least 95% identical to an amino acid sequence chosen from SEQ ID NO:1, 2, 3, 19, 20, 21, 47, 48, 49, 65, 66, 67, 83, 84, 85, 101, 102, 103, 119, 120, 121, 137, 138 and 139, wherein the antibody selectively binds to an IL-21 receptor.
2. An isolated antibody encoded by a nucleotide sequence which is at least 95% identical to a nucleotide sequence chosen from SEQ ID NO:10, 11, 12, 28, 29, 30, 56, 57, 58, 74, 75, 76, 92, 93, 94, 110, 111, 112, 128, 129, 130, 146, 147, and 148, wherein the antibody selectively binds to an IL-21 receptor.
3. An isolated antibody comprising a V_H domain having an amino acid sequence which is at least 95% identical to an amino acid sequence chosen from SEQ ID NO:1, 19, 47, 65, 83, 101, 119 and 137, and a V_L domain having an amino acid sequence which is at least 95% identical to an amino acid sequence chosen from SEQ ID NO:2, 20, 48, 66, 84, 102, 120 and 138, wherein the antibody selectively binds to an IL-21 receptor.
4. An isolated antibody comprising a V_H domain which comprises one or more CDRs chosen from SEQ ID NO:4, 5, 6, 22, 23, 24; 50, 51, 52, 68, 69, 70, 86, 87, 88, 104, 105, 106, 122, 123, 124, 140, 141, 142 and conservative amino acid substitutions thereof, wherein the antibody selectively binds to an IL-21 receptor.

5. An isolated antibody comprising a V_L domain which comprises one or more CDRs chosen from SEQ ID NO:7, 8, 9, 25, 26, 27, 53, 54, 55, 71, 72, 73, 89, 90, 91, 107, 108, 109, 125, 126, 127, 143, 144, 145 and conservative amino acid substitutions thereof, wherein the antibody selectively binds to an IL-21 receptor.
6. An isolated antibody that competes with an antibody comprising an amino acid sequence chosen from SEQ ID NO:1, 2, 3, 19, 20, 21, 47, 48, 49, 65, 66, 67, 83, 84, 85, 101, 102, 103, 119, 120, 121, 137, 138 and 139, for binding to an IL-21 receptor.
7. An isolated antibody which binds the same epitope on an IL-21 receptor as an antibody comprising an amino acid sequence chosen from SEQ ID NO:1, 2, 3, 19, 20, 21, 47, 48, 49, 65, 66, 67, 83, 84, 85, 101, 102, 103, 119, 120, 121, 137, 138 and 139.
8. The antibody of claim 1, 2, 3, 4, 5, 6 or 7, wherein the antibody selectively binds to an amino acid sequence that is at least 95% identical to a sequence comprising at least 100 contiguous amino acids set forth in SEQ ID NO:43.
9. The antibody of claim 1, 2, 3, 4, 5, 6 or 7, wherein the antibody selectively binds the extracellular domain of human IL-21 receptor.
10. The antibody of claim 1, 2, 3, 4, 5, 6 or 7, wherein the antibody inhibits the binding of IL-21 to an IL-21 receptor.
11. The antibody of claim 1, 2, 3, 4, 5, 6 or 7, wherein the antibody is human.

12. The antibody of claim 1, 2, 3, 4, 5, 6 or 7, wherein the antibody is an IgG₁ antibody.
13. The antibody of claim 12, wherein the antibody is IgG_{1λ} or IgG_{1κ}.
14. An isolated antibody expressed by a host cell having ATCC Deposit Designation No. PTA-5030 or PTA-5031.
15. A pharmaceutical composition comprising the antibody of claim 1, 2, 3, 4, 5, 6 or 7.
16. An isolated nucleic acid encoding the antibody of claim 1, 2, 3, 4, 5, 6 or 7.
17. An expression vector comprising the nucleic acid of claim 16.
18. A host cell transformed with the vector of claim 17.
19. The host cell of claim 18, wherein the host cell is a bacteria, mammalian cell, yeast cell, plant cell, or an insect cell.
20. A host cell having ATCC Deposit Designation No. PTA-5030 or PTA-5031.
21. A method of producing an antibody that binds to an IL-21 receptor, comprising culturing the host cell of claim 20 under conditions that allow expression of the antibody, and isolating the antibody from the cell culture.
22. A method of generating an antibody or antigen-binding fragment that selectively binds an IL-21 receptor comprising:

- (a) providing a repertoire of nucleic acids encoding a variable domain that either includes a CDR 1, 2 or 3 to be replaced or lacks a CDR1, 2 or 3 encoding region;
 - (b) combining the repertoire with a donor nucleic acid encoding an amino acid sequence substantially as set forth in SEQ ID NO:4, 5, 6, 7, 8, 9, 22, 23, 24, 25, 26, 27, 50, 51, 52, 53, 54, 55, 68, 69, 70, 71, 72, 73, 86, 87, 88, 89, 90, 91, 104, 105, 106, 107, 108, 109, 122, 123, 124, 125, 126, 127, 140, 141, 142, 143, 144 or 145, such that the donor nucleic acid is inserted into the CDR1, 2 or 3 region in the repertoire, so as to provide a product repertoire of nucleic acids encoding a variable domain;
 - (c) expressing the nucleic acids of said product repertoire;
 - (d) selecting an antigen-binding fragment specific for the IL-21 receptor; and
 - (e) recovering the antigen-binding fragment or nucleic acid encoding the antigen-binding fragment.
23. An antibody produced by the method of claim 22.
24. The method of claim 22, further comprising the step of germlining.
25. A method of regulating an immune response comprising contacting a cell with the antibody of claim 1, 2, 3, 4, 5, 6, 7 or 23, thereby regulating the immune response.
26. The method of claim 25, wherein the cell is a leukocyte or a synovial cell.

27. The method of claim 26, wherein the leukocyte is a T cell, a B cell, a NK cell, or a macrophage.
28. The method of claim 25, wherein the immune response comprises cell proliferation, cytolytic activity, cytokine secretion, or chemokine secretion.
29. A method of treating or preventing an immune cell-associated disorder, in a subject, comprising, administering to the subject the antibody of claim 1, 2, 3, 4, 5, 6, 7 or 23, in an amount sufficient to inhibit or reduce immune cell activity in the subject, thereby treating or preventing the disorder.
30. The method of claim 29, wherein the immune cell-associated disorder is chosen from multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, juvenile rheumatoid arthritis, osteoarthritis, psoriatic arthritis, ankylosing spondylitis, transplant rejection, inflammatory bowel disease, psoriasis and Crohn's disease.
31. The method of claim 30, wherein the immune cell-associated disorder is chosen from rheumatoid arthritis, inflammatory bowel disease, Crohn's disease and psoriasis.
32. The method of claim 29, further comprising administering to the subject another therapeutic agent chosen from a cytokine inhibitor, a growth factor inhibitor, an immunosuppressant, an anti-inflammatory agent, a metabolic inhibitor, an enzyme inhibitor, a cytotoxic agent, and a cytostatic agent.
33. The method of claim 32, wherein the therapeutic agent is chosen from a TNF antagonist, an IL-12 antagonist, an IL-15 antagonist, an IL-17 antagonist, an IL-18 antagonist, an IL-22 antagonist, a T cell depleting agent, a B cell

depleting agent, methotrexate, leflunomide, rapamycin, or an analog thereof, a Cox-2 inhibitor, a cPLA2 inhibitor, an NSAID, and a p38 inhibitor.

34. A method of treating or preventing a hyperproliferative disorder, in a subject, comprising administering to the subject the antibody of claim 1, 2, 3, 4, 5, 6, 7 or 23, in an amount sufficient to inhibit or reduce hyperproliferation of IL-21- and/or IL-21 receptor-responsive cells in the subject, and allowing the antibody to treat or prevent the disorder.
35. The method of claim 34, wherein the subject is a mammal.
36. The method of claim 34, wherein the subject is a human.
37. The method of claims 29, 30 or 33, wherein the antibody is administered in a range chosen from 1 μ g/kg to 20 mg/kg, 1 μ g/kg to 10 mg/kg, 1 μ g/kg to 1 mg/kg, 10 μ g/kg to 1 mg/kg, 10 μ g/kg to 100 μ g/kg, 100 μ g to 1 mg/kg, and 500 μ g/kg to 1 mg/kg.
38. A diagnostic kit comprising the antibody of claim 1, 2, 3, 4, 5, 6, 7 or 23.